

N^o 20,188



A.D. 1901

Date of Application, 9th Oct., 1901

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PROVISIONAL SPECIFICATION.

Improvement in the Manufacture of Salicylide or Salicylic Anhydride.

I, JASPER WETTER, Chartered Patent Agent, of 37 & 39, Essex Street, Strand, London, do hereby declare the nature of this invention, a communication from the Firm of F. Hoffmann-la Roche & Co, Manufacturers, of Bale, Switzerland, to be as follows:—

5 The present invention has for its object, to produce pure salicylide suitable for pharmaceutical and other purposes.

If acetyl-salicylic acid is heated, it will yield salicylide already at a temperature of 150—160, while giving off acetic acid, but for completing the reaction, that is obtaining almost the theoretical quantity of salicylide, it is necessary to
10 work at a temperature between 200 and 210° C.

The product thus obtained is a thick liquid when hot, but rapidly solidifies on cooling, so that it can be easily pulverised.

In order to get rid of any aceto-salicylic acid adhering to it and also of reconstituted salicylic acid, the product is repeatedly boiled with water or with dilute
15 spirits, and then dissolved in benzene, glacial acetic acid or chloroform, but preferably in acetone, after which the salicylide is precipitated out of the saturated acetone solution, preferably by pouring the solution into cold water.

Pure salicylide is a white tasteless powder, practically insoluble in water and in ether, very sparingly soluble in hot alcohol. Its composition is represented
20 by the formula $C_7H_4O_2$.

If the salicylide is dissolved in boiling alcohol, the solution does not give the chemical reactions of salicylic acid. Salicylide is easily soluble in chloroform, glacial acetic acid, benzene, and especially in acetone. When heated to 110° C, it begins to sinter, at 130° it assumes the consistency of wax, at 160° it
25 is a thick liquid, and at 210° it begins to melt. It cannot be distilled without decomposition.

When boiled with caustic alkalies, it rapidly and easily forms a salicylate and enters completely into solution. Alkali-carbonates decompose it, they will even decompose it in a 2—5 *per cent* solution and at ordinary temperature if allowed
30 to stand for a considerable time.

With the exception of concentrated sulphuric acid, which converts it into sulpho-salicylic acid, acids will not split it up. In nitric acid it dissolves while forming trinitric-salicylide. The latter may be crystallised out of water in the shape of fine crystals which melt at 121.5° and taste very bitter.

35 Solutions of the nitric compound will not react with chloride of iron.

The therapeutic value of pure salicylide is based on the fact, that it will not injure or disagree with the stomach, that it is free from disagreeable secondary effects, and will reconstitute salicylic acid only, when in contact with the walls of the duodenum.

40 Dated this 9th day of October 1901.

FAIRFAX & WETTER,
Agents for the Applicant.

Wetter's Improvement in the Manufacture of Salicylide or Salicylic Anhydride.

COMPLETE SPECIFICATION.

Improvement in the Manufacture of Salicylide or Salicylic Anhydride,

I, JASPER WETTER, Chartered Patent Agent, of 37 and 39, Essex Street, Strand, London, do hereby declare the nature of this invention and what manner the same is to be performed, a communication from the Firm of F. Hoffmann-la Roche & Co., Manufacturers, of Bale, Switzerland, to be particularly described and ascertained in and by the following statement:—

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The present invention has for its object, to produce pure salicylide suitable for pharmaceutical and other purposes.

If acetyl-salicylic acid is heated, it will yield salicylide already at a temperature of 150—160° C, while giving off acetic acid, but for completing the reaction, that is obtaining almost the theoretical quantity of salicylide, it is necessary to work at a temperature between 200 and 210° C.

10

The product thus obtained is a thick liquid, when hot, but rapidly solidifies on cooling, so that it can be easily pulverised.

In order to get rid of any aceto-salicylic acid adhering to it and also of reconstituted salicylic acid, the product is repeatedly boiled with water or with dilute spirits, and then dissolved in benzene glacial acetic acid or chloroform, but preferably in acetone, after which the salicylide is precipitated out of the saturated acetone solution, preferably by pouring the solution into cold water.

15

Pure salicylide is a white tasteless powder, practically insoluble in water and in ether, very sparingly soluble in hot alcohol. Its composition is represented by the formula $C_7H_4O_2$.

20

If the salicylide is dissolved in boiling alcohol, the solution does not give the chemical reactions of salicylic acid. Salicylide is easily soluble in chloroform, glacial acetic acid, benzene, and especially in acetone. When heated to 110° C, it begins to sinter, at 130° it assumes the consistency of wax, at 160° it is a thick liquid, and at 210° it begins to melt. It cannot be distilled without undergoing decomposition.

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When boiled with caustic alkalies, it rapidly and easily forms a salicylate and enters completely into solution. Hot alkali carbonates decompose it, they will even decompose it in a 2—5 *per cent* solution and at ordinary temperature, if allowed to stand for a considerable time.

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With the exception of concentrated sulphuric acid, which converts it into sulpho-salicylic acid, acids will not split it up. In nitric acid it dissolves while forming trinitro-salicylide. The latter may be crystallised out of water in the shape of fine crystals, which melt at 121.5° and taste very bitter.

35

Solutions of the nitric compound will not react with chloride of iron.

The therapeutic value of pure salicylide is based on the fact, that it will not injure or disagree with the stomach, that it is free from disagreeable secondary effects, and will reconstitute salicylic acid only, when in contact with the walls of the duodenum.

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EXAMPLE.

10 kilogrammes of aceto-salicylic acid in an open vessel are slowly heated to a temperature ranging between 200 and 210° C. and maintained at that temperature for 5 to 6 hours, in order to complete the reaction.

The product is allowed to cool, the crude salicylide thus obtained (from 6.3 to 6.5 kilos) is crushed and extracted two or three times with 4 to 6 times its quantity of water.

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The product (which has the property of hardening rapidly) is then dissolved in 4 to 5 times its quantity of acetone, and the clear solution is poured into 20

Wetter's Improvement in the Manufacture of Salicylide or Salicylic Anhydride.

to 30 its quantity of water, thereby causing the salicylide to separate in the shape of white cheese-like flakes which are subsequently dried.

Having now particularly described and ascertained the nature of my said invention, and in what manner the same is to be performed, I declare that what
5 I claim is:—

1. The process for obtaining salicylide, which consists in heating aceto-salicylic acid to 200—210° for a considerable time, boiling the product of the reaction with water, subsequently dissolving it in acetone or similar solvent, and finally precipitating with water, substantially as described.
- 10 2. The method of producing salicylide, substantially as described.
3. Pure salicylide having the properties described and obtainable in the manner substantially as described.

Dated this 30th day of June 1902.

15 FAIRFAX & WETTER,
Agents, 37 and 39, Essex Street, Strand, London.

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